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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/752,423	01/06/2004	Erik Buntinx	29248/19	3783
1912 7590 10/02/2007 AMSTER, ROTHSTEIN & EBENSTEIN LLP 90 PARK AVENUE NEW YORK, NY 10016			EXAMINER RAMACHANDRAN, UMAMAHESWARI	
			ART UNIT 1617	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/752,423

Applicant(s)

BUNTINX, ERIK

Examiner

Umamaheswari Ramachandran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-4 and 6-10 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 6-10 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

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DETAILED ACTION

Applicants' election of group I, claims 1-10, a) anxiety disorders for a species of disorder and (b) pipamperone for a species of compound in the reply filed on 7/10/2007 is acknowledged. Claims 1-4, 6-10 read on the elected species. Claim 5 is cancelled. Claims 11-63 are withdrawn from consideration. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Thus the restriction requirement elected is made final. Claims 1-4, 6-10 are pending and are being examined on the merits herein.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4 and 6-9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-4 and 42 of copending Application No. 10/984,683.

Claims 1-4 and 6-9 of the instant application is drawn to a method of for treating a disease or disorder such as anxiety disorder comprising administering to a patient a

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compound such as pipamperone and a second agent such as serotonin reuptake inhibitor.

Claims 1-4 and 42 of co-pending application ('683) teach a method for treating a disease or disorder with an underlying dysregulation of the emotional functionality that include anxiety disorders, mood disorders etc. comprising, administering to a patient pipamperone simultaneously with, separate from or sequential to second compound to augment the therapeutic effect or to provide a faster onset of the therapeutic effect of said second compound. The application teaches that second compound can be a selective serotonin reuptake inhibitor.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both teach a method of treatment of emotional disorders such as anxiety disorder comprising administering pipamperone and a selective serotonin reuptake inhibitor as a second agent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-4, 6-10 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 82-84, 100, 101 of copending Application No. 10/580,962.

Claims 1-4, 6-10 of the instant application is drawn to a method of for treating a disease or disorder such as anxiety disorder comprising administering to a patient a compound such as pipamperone and a second agent, citalopram, a serotonin reuptake inhibitor.

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Claims 82-84, 100,101 of the co-pending application ('962) teach a method for treating mood disorders or anxiety disorders comprising administering to a patient pipamperone, or a pharmaceutically acceptable salt thereof, in a dose ranging between 5 and 15 mg per day of the active ingredient, and administering said pipamperone simultaneously with, separate from or sequential to a second compound, to augment the therapeutic effect of said second compound or to provide a faster onset of the therapeutic effect of said second compound, wherein said second compound is selected from the group consisting of: selective serotonin, nor-adrenaline and dopamine re-uptake inhibitors (SNDRI), selective serotonin and nor-adrenaline re-uptake inhibitors (SNRI) and selective serotonin re-uptake inhibitors (SSRI). The co-pending application further teaches escitalopram, fluoxetine etc to be a second agent.

Although the conflicting claims are not identical, they are not patentably distinct from each other because both teach a method of treatment of emotional disorders such as anxiety disorder comprising administering pipamperone and a selective serotonin reuptake inhibitor such as citalopram as a second agent.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 1-4, 6-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The specification teach measuring pKi values of some test compounds and describes the foregoing pipamperone-citalopram treatment for depressive disorder clinical trial set up data but do not show any real data or examples of treating a disorder such as anxiety disorder administering to a patient a compound such as pipamperone and citalopram. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification does not provide support to the subject matter of the claimed invention of treating a disease or a disorder with an underlying dysregulation of the emotional functionality comprising administering a compound that has selective affinity for dopamine D4 receptor and a selective affinity for 5-HT2A receptor.

Claims 1-4, 6-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification teach measuring pKi values of some test compounds and describes the foregoing pipamperone-citalopram treatment for depressive disorder clinical trial set up data does not reasonably provide enablement for disorders listed in claim 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

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The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the Invention:

The rejected claims are drawn to a method of treating an array of disorders (listed in claim 3) that includes anxiety disorder, somatoform disorders, behavior disorders, eating disorders etc. comprising administering a compound that has selective affinity for dopamine D4 receptor and a selective affinity for 5-HT2A receptor.

(2) Breadth of the claims:

Claim 1 is broad as it is drawn to a method treating a disease or disorder with an underlying dysregulation of the emotional functionality comprising administering a compound that has selective affinity for dopamine D4 receptor and a selective affinity for 5-HT2A receptor. Claim 3 is limited to a list of disorders. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

(3) Guidance of the Specification:

The guidance given by the specification is for measuring pKi values of some test compounds and description of the foregoing pipamperone-citalopram treatment for depressive disorder clinical trial set up.

(4) Working Examples:

The specification provide set up data for the clinical trial for a method of treatment of depressive disorder.

(5) The relative skill of those in the art:

The relative skill of those in the medical treatment art is high, requiring advanced education and training.

(6) The predictability of art:

The method claim of treatment of a disease or a disorder with an underlying dysregulation of the emotional functionality comprising administering a compound that has selective affinity for dopamine D4 receptor and a selective affinity for 5-HT2A receptor is so broad and there is a high degree of unpredictability involved. Despite the advanced training in the medical treatment arts, the arts are highly unpredictable.

(7) The Quantity of Experimentation Necessary:

In order to practice the above claimed invention, one of skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system to test every single compound for the affinity of dopamine and 5-HT2A receptors and then determine whether or not they are useful in the treatment of every disease or disorder with an underlying dysregulation of the emotional functionality as claimed in claim 1 or the disorders listed in claim 3. Prior

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to such testing in the animal model in vitro determination of the affinity of the compounds towards dopamine D4 and 5HT2A receptors needs to be conducted. If unsuccessful, one of skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of comprising administering compounds with selective affinity towards dopamine D4 receptors and 5-HT2A receptors in a method of treatment of a disease or a disorder with an underlying dysregulation of the emotional functionality. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claims 1-4, 6-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification teach measuring pKi values of some test compounds and describes the foregoing pipamperone-citalopram treatment for depressive disorder clinical trial set up data does not reasonably provide enablement for any other compound that has selective affinity for dopamine D4 receptor and a selective affinity for 5-HT2A receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The nature of the Invention:

The rejected claims are drawn to a method of treating a disease or disorder with an underlying dysregulation of the emotional functionality comprising administering a compound that has selective affinity for dopamine D4 receptor and a selective affinity for 5-HT2A receptor.

(2) Breadth of the claims:

Claim 1 is broad as it is drawn to a method treating a disease or disorder with an underlying dysregulation of the emotional functionality comprising administering a compound that has selective affinity for dopamine D4 receptor and a selective affinity for 5-HT2A receptor. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

(3) Guidance of the Specification:

The guidance given by the specification is for measuring pKi values of some test compounds and description of the foregoing pipamperone-citalopram treatment for depressive disorder clinical trial set up.

(4) Working Examples:

The specification provide set up data for the clinical trial for a method of treatment of depressive disorder.

(5) The relative skill of those in the art:

The relative skill of those in the medical treatment art is high, requiring advanced education and training.

(6) The predictability of art:

The method claim of treatment of a disease or a disorder with an underlying dysregulation of the emotional functionality comprising administering a compound that has selective affinity for dopamine D4 receptor and a selective affinity for 5-HT2A receptor is so broad and there is a high degree of unpredictability involved. Despite the advanced training in the medical treatment arts, the arts are highly unpredictable.

(7) The Quantity of Experimentation Necessary:

In order to practice the above claimed invention, one of skill in the art would have to first envision formulation, dosage, duration, route and, in the case of human treatment, an appropriate animal model system to test every single compound for the affinity of dopamine and 5-HT2A receptors and then determine whether or not they are useful in the treatment of a disorder such as anxiety disorder. Prior to such testing in the animal model in vitro determination of the affinity of the compounds towards dopamine

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D4 and 5HT2A receptors needs to be conducted. If unsuccessful, one of skill in the art would have to envision a modification in the formulation, dosage, duration, route of administration etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention of comprising administering compounds with selective affinity towards dopamine D4 receptors and 5-HT2A receptors in a method of treatment of a disorder such as anxiety disorder. Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 6-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dudley et al. (US 2004/0002482) in view of Dodman (U.S. 5,762,960) and further in view of Sanchez (U.S. 2002/0086899).

Dudley et al. teach methods for treating or reducing the symptoms of a depressive disorder (abstract). Dudley et al. further teach the compounds pipamperone and the SSRI citalopram, in combination, can be used in the method (pages 9-10, paragraph [0132]). The compositions and therapeutic agents are administered simultaneously or sequentially for a daily administration from about 0.1 g to about 10 g (page 12, paragraphs [0158] - [0172]). Dudley et al. teach mood disorder to be a depressive disorder (page 13, paragraph 0187) and further psychological anxiety as one of the psychological aspects of depression (p 59, para 523).

The reference does not explicitly teach the use of pipamperone in the treatment of anxiety disorder (elected species).

Dodman teach the neuroleptic substance, pipamperone serves to alleviate the anxious state of mind and reduce mental anxiety (col. 10, lines 20-21).

Dudley and Dodman do not explicitly teach the use of citalopram in the treatment of anxiety disorder (elected species).

Sanchez teach the use of escitalopram (s-enantiomer of citalopram, 40 mg/kg) in the treatment of neurotic disorders including anxiety disorder, social anxiety disorder etc. (See Abstract).

It would have been obvious to one of ordinary skill in the art at the time of the invention to make a composition comprising a compound such as pipamperone and

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citalopram in a method of treatment of a disease or a disorder such as anxiety disorder because of the teachings of Dudley, Dodman and Sanchez. Dudley teaches compounds pipamperone and SSRI citalopram in combination to be useful in a method of treating depression. The reference further teaches psychological anxiety as one of the psychological aspects of depression. Dodman teach the neuroleptic substance, pipamperone serves to alleviate the anxious state of mind and reduce mental anxiety and Sanchez teach the use of citalopram in the treatment of anxiety disorders. Hence one of ordinary skill in the art would have been motivated to use pipamperone and citalopram in a combination therapy for the treatment of a disease or a disorder such as anxiety disorder due to expectation of synergistic effects and therapeutic benefits as both the compounds have been shown to be useful in a method of treatment of condition like anxiety disorder. Regarding the daily dose of pipamperone in the composition as recited in claims 1 and 42, it is noted that Dudley et al. teach the compositions and therapeutic agents are administered at a daily dose from about 0.1 g to about 10 g, which closely meets the daily dose of pipamperone in the composition set forth in claims 1 and 40 (page 12, paragraph [0158]). It is considered that one of ordinary skill in the art at the time the invention was made would have found it obvious to vary and/or optimize the amount of pipamperone provided in a composition, according to the guidance set forth in Dudley et al., to provide a composition having the desired daily dose of pipamperone. It is noted that "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or

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workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 223,235 (CCPA 1955).

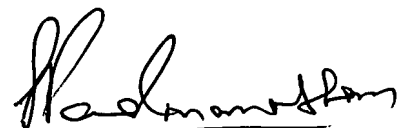
Conclusion

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Umamaheswari Ramachandran whose telephone number is 571-272-9926. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



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SUPERVISORY PATENT EXAMINER